UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,649	02/16/2006	Giorgio Terenghi	TEPH109	4566

23579 7590 08/19/2008

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361

EXAMINER	
WANG, CHANG YU	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
08/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/568,649
Filing Date: February 16, 2006
Appellant(s): TERENGHI ET AL.

Patrea L. Pabst
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 3, 2008 appealing from the Office action mailed October 23, 2007

It is noted that Appellant submitted an IDS after final. The IDS submitted on 5/30/08 is not entered because it constitutes new evidence and fails to comply with 37 CFR 1.97(d) because it lacks a statement as specified in 37 CFR 1.97(e) and also lacks the fee set forth in 37 CFR 1.17(p). See MPEP 609.04-(b)-III & 37CFR 1.197 for proper submission of IDS after final.

In addition, Appellant states that the listed references in the section of Evidence Appendix in the Appeal brief were listed in the IDS filed August 30, 2006. However, Appellant's statement is incorrect because the cited PCT references in the Evidence Appendix were not listed in the IDS filed August 30, 2006, and thus are not considered.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

The rejection of claims 1 and 3-6 under 35 U.S.C. 112, second paragraph, as being indefinite because of the recitation "suitable" is withdrawn.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6548569	Williams et al.	04-2003
6610764	Martin et al.	08-2003
6838493	Williams et al.	01-2005
7179883	Williams et al.	02-2007

5584885	Seckel	12-1996
6867247	Williams et al.	03-2005
US2002/0156150	Williams et al.	10-2002
US2002/0173558	Williams et al.	11-2002
US2004/0234576	Martin et al.	11-2004
US2006/0058470	Rizk	03-2006
WO01/54593	Hadlock et al.	08-2001

Martin et al. "Medical applications of poly-4-hydroxybutyrate: a strong flexible absorbable biomaterial" Biochemical Engineering Journal, 2003. 16: 97-105.

Schlossauer et al. "Synthetic nerve guide implants in humans: a compreshensive survey" Neurosurgery, 2006. 59:740-748.

Clavijo-Alvarez et al. "Comparison of biodegradable conduits within aged rat sciatic nerve defects" Plast. Reonstr. Surg. 2007. 119:1839-1851.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

A. Claims 1 and 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/54593 (Hadlock et al., published on Aug 2, 2001) in view of Martin et al. (Biochem. Eng. J. 2003. 97-105).

Claims 1 and 3-6 are drawn to a nerve regeneration device comprising a polyhydroxyalkanoate (PHA) polymer in the form of a porous conduit tube or sheet for nerve repair wherein the pores in the conduit have a diameter of between 5-500microns (i.e. μM) and wherein the polymer comprises 4-hydroxybutyrate (4-HB or P4HB) and wherein the conduit does not comprises or comprises a material selected from the group consisting of nerve cells, growth factors and drugs.

WO 01/54593 teaches a nerve regeneration conduit comprising biodegradable polymers selecting from polyhydroxyalkanoate (PHA), polyhydroxybutyric acid and polyesters as recited in instant claim 1(see p. 2, line 1-p.4, line 13; p.6, line 12-p. 7, line 28; p. 13, claims 1-8, in particular). WO01/54593 also teaches that the conduit comprises Schwann cells (i.e. one type of nerve cells) or neurotrophic agents (i.e. growth factors and drugs) as recited in instant claim 6 (see p. 4, lines 1-14; p. 8, line 12-p. 9, line 20; p. 14, claims 9-12; p. 16, claim 29-30, in particular), and the thickness

of the conduit is 5-200μm (see p.2-4, in particular). WO01/54593 also teaches the pore size is about 10-100μm (see p.7, lines 25-27, in particular). But WO01/54593 fails to teach 4-hydroxybutyrate and pore size of 5-500μm in diameter as recited in instant claim 1.

Martin et al. teach that poly-4-hydroxybutyrate (P4HB) is polyester that belongs to the class of polyhydroxyalkanoate (PHA) and is used for tissue regeneration (see p.97, 1st col. 1st paragraph; 2nd col. 1st paragraph, in particular). Martin et al. also teach P4HB patches (i.e. sheet) with a pore size of 180-240μm, which is within the limitation recited in instant claims 1, 3 and 5 (see p. 100, 1st col. 2nd paragraph, in particular). Martin et al. further teach that P4HB is more flexible, more stable to hydrolysis than P3HB, and useful for tissue engineering (p. 98, 2nd col., 3-4th paragraphs; p.100, 1st col., 2nd paragraph, in particular) and its metabolite, 4HB is naturally present in human brain and other tissues. Martin et al. teach that PHA polymers including P3HB and its copolymers are successful in use of peripheral nerve repair (p. 105, 1st col., 2nd paragraph, in particular). The teachings of Martin et al. provide a motivation and an expectation of success in use P4HB to replace P3HB in PHA polymers for peripheral nerve regeneration because PHA polymers have been used to generate a nerve regeneration conduit and P4HB is more stable and useful than P3HB for tissue regeneration

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to combine the teachings of WO 01/54593 and Martin et al. to make a nerve regeneration conduit comprising PHA wherein the PHA comprises

P4HB. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because PHA and P3HB have successfully been used for peripheral nerve repair and P4HB is more stable to hydrolysis in tissue engineering.

B. Claims 1 and 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6548569 (Williams et al., issued on Apr 15, 2003, priority date Mar 25, 1999) in view of US. Patent No. 5584885 (Seckel, issued on Dec 17, 1996) and evidentiary references Schlossauer. (Neurosurgery, 2006. 59:740-748) and Clavijo-Alvarez et al. (Plast. Reconstr. Surg. 2007. 119:1839-1851).

Claims 1 and 3-6 are drawn to a nerve regeneration device comprising a polyhydroxyalkanoate polymer comprising 4-hydroxybutyrate (4HB or P4HB) in the form of a porous conduit tube or sheet and having a diameter of between 5 and 500 microns (μm) and wherein the conduit does not comprises or comprises a material selected from the group consisting of nerve cells, growth factors and drugs.

US Patent No. 6548569 (the '569 patent) teaches devices of tissue regeneration or nerve guidance/regeneration made of biocompatible polyhydroxyalkanoates (PHA) comprising poly-4-hydroxybutyrate (P4HB) as recited in instant claims 1 and 3 (see col. 4, lines 20-57; col.7, lines 31-35, in particular). The '569 patent teaches a biodegradable device comprising a polyhydroxyalkanoate (PHA) polymer comprising 4-hydroxybutyrate as a preferred embodiment (see col.7, lines 31-35, in particular) in a form of porous conduit such as having the shape of the nerve conduit products of

NEUROTUBE™ as incorporated by the references including US Patent NOs. 5735863, 5584885 and 5026381 (see col. 16, lines 42-52, in particular). The '569 patent teaches that the pore size of PHA is between nanometers to 500μm in diameter by using pore forming agents or particles with diameters between nanometers to 500 microns as recited in instant claims 1 and 4-5 (see col. 10, lines 31-42, in particular). The '569 patent also teaches the process of forming pore size of 80-180μm for nerve conduits made of P4HB using pore forming agents or particles (sodium chloride crystals) with diameters between 80-180μm, which is within the recited range (see col.33, example 4; col. 37, example 6, in particular).

In addition, the 569 patent teaches that the nerve guides can be fabricated based on the teaching of several incorporated patents as described above. For example, US Patent No. 5584885 (i.e. one of the incorporated references in the '569 patent as described above) teaches nerve guides (i.e. nerve conduits) comprising Schwann cells, growth factors and drugs as recited in instant claim 6 (see col.7, line18-col.8, line 29; col. 16, lines 22-60 of the '885 patent, in particular).

Furthermore, the size of nerve conduits of NEUROTUBE™ recited in the '569 patent is a tube with 2-8mm in diameter and 4cm in length and having the pore size of 30-50μm in diameter, which is within the limitation recited in instant claim 1, as evidenced by Schlosshauer (see p. 742, table 2, Schlossauer. Neurosurgery, 2006. 59:740-748) and Clavijo-Alvarez et al. (see p. 1840, 3rd paragraph; Clavijo-Alvarez et al. Plast. Reconstr. Surg. 2007. 119:1839-1851).

Although the '569 patent does not teach the pore size between 5μm-500μm diameter, the range of pore size recited in the instant claims is obvious over the '569 patent because the claimed ranges (i.e. 5-500μm) overlap or lie inside the ranges disclosed by the '569 patent (i.e. nanometer-500μm). Note that

"where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)", See MPEP 2144.05-I.

Moreover, the '569 patent shows that both of the conduits having the pore size with the ranges between nanometer-500μm and between 80-180μm in diameter are effective in promoting nerve regeneration. The claimed pore size range between 5μm-500μm of the claimed conduit is an obvious variant because both of the conduits with a broader range (nanometer-500um) and a narrower range (80-180) of the pore size have the same effects on nerve regeneration. The claimed conduits with the claimed pore size in the instant claims would predictably have the same effect or result in nerve regeneration as in the prior art. Note that

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II.

Thus, it would have been obvious to a skilled artisan at the time the instant invention was made to apply the teaching of the '885 to the teaching of the '569 patent to generate a nerve regeneration device comprising P4HB polymers in the form of porous conduit tube or sheet having a pore size between 5-500 mm and further comprises materials to enhance nerve regeneration. The skilled artisan would have

been motivated with an expectation of success in making the claimed conduit because the '569 patent teaches a biodegradable composition or device comprising P4HB in a shape of Neurobute™ or sheet with a pore size between nanometer-500mm for nerve guides and the 885 patent teaches several Schwann cells, growth factors and drugs can be incorporated into the nerve guides.

C. Claims 1 and 3-6 are rejected under 35 U.S.C. 103 (a) as being unpatentable over U.S. Patent No. 6610764 (issued on Aug 26, 2003, priority date Nov 17, 1997), US 6838493 (issued on Jan 4, 2005, priority date Mar 25, 1999), US 6867247 (issued Mar 15, 2005, priority date Mar 25,1999), US 7179883 (issued on May 19, 2005, priority date Mar 25, 1999), US2002/0156150 (US Application No. 10/082954, published Oct 24, 2002) or US2002/017358 (US Application No. 10/136499, published Nov 21, 2002) each in view of Seckel (US. Patent No. 5584885, issued on Dec 17, 1996) and evidentiary references Schlossauer. (Neurosurgery, 2006. 59:740-748) and Clavijo-Alvarez et al. (Plast. Reconstr. Surg. 2007. 119:1839-1851). The reasons of the rejection are as set forth above at paragraph B and in the section of double patenting since these cited references share the same specification with that of US 6548569.

The issued patents US 6610764, US 6838493, US 6867247, US 7179883 and copending applications US2002/0156150 (US Application No. 10/082954) and US2002/017358 (US Application No. 10/136499) teach a biocompatible polyhydroxyalkanoate composition, or a device or a polymeric filament or fiber for a medical device comprising 4-hydroxybutyrate polymers for different medical uses

including nerve regeneration. These specifications teach a biodegradable device comprising a polyhydroxyalkanoate comprising 4-hydroxybutyrate in a form of porous conduit such as having the shape of the nerve conduit products of NEUROTUBE™ as incorporated by the references and having the pore size of PHA between nanometers to 500μm or 80-180μm in diameter, which is within the range of a pore size of 5-500μm in diameter in the form of a tube as recited in instant claims 1 and 3-5. US Patent No. 5584885 (i.e. one of the incorporated references) teaches nerve guides (i.e. nerve conduits) comprising Schwann cells, growth factors and drugs as recited in instant claim 6 (see col.7, lines18-col.8, lines 29; col. 16, lines 22-60, in particular). The size of nerve conduits of NEUROTUBE™ is a tube with 2-8mm in diameter and 4cm in length and having the pore size of 30-50μm in diameter, which is within the limitation recited in instant claim 1, as evidenced by Schlosshauer (see p. 742, table 2, Schlossauer. Neurosurgery, 2006. 59:740-748) and Clavijo-Alvarez et al. (see p. 1840, 3rd paragraph; Clavijo-Alvarez et al. Plast. Reconstr. Surg. 2007. 119:1839-1851). Thus, the claimed conduit is obvious over the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

D. Claims 1 and 3-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1-34 of U.S. Patent No. 6610764, claims 1-4 and 6-28 of US 6838493, claims 1-3 and 5-20 of US 6548569, claims 1-4 and 6-30 of US 6867247 and claims 30 and 35-61 (original claims, now claims 1-31) of US 7179883. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1 and 3-6 of the instant application encompass a nerve regeneration device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate and the conduit comprises nerve cells, growth factors or drugs. Claims 1-34 of the '764 patent encompass a biocompatible polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the biocompatible composition comprises active agents including growth factors and drugs. Claims 1-4 and 6-28 of the '493 patent encompass a device comprising a biodegradable polyhydroxyalkanoate polymer composition comprising a polymer selecting from poly-4-hydroxybutyrate, poly-4-hydroxybutyrate-co-3-hydroxybutyrate, poly-4-hydroxybutyrate-co-2-hydroxybutyrate and copolymers thereof, and the composition also comprises active agents including growth factors and drugs.

Claims 1-3 and 5-20 of the '569 patent encompass a biodegradable polyhydroxyalkanoate composition selecting from poly-4-hydroxybutyrate, poly-4-hydroxybutyrate-co-3-hydroxybutyrate, poly-4-hydroxybutyrate-co-2-hydroxybutyrate and copolymers thereof. Claims 1-4 and 6-30 of the '247 patent encompass a biocompatible polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the biocompatible composition comprises active agents including growth factors and drugs, and the device comprising the biocompatible composition for different medical uses including nerve regeneration. Claims 30 and 35-61 (i.e. original claims, now claims 1-31) of the '883 patent encompass a device for different medical uses comprising a biodegradable polyhydroxyalkanoate composition comprising poly-4-hydroxybutyrate and the device also comprises different drugs for medical use including nerve regeneration. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same composition comprising a polyhydroxyalkanoate polymer comprising 4-hydroxybutyrate. In addition, the poly-4-hydroxybutyrate encompasses 4-hydroxybutyrate with one or more different hydroxy acid units. Furthermore, although the claims in the issued patent do not specifically recite the pore size between 5-500μm and the shape, the working examples in these issued patents teach conduits and sheets and the pore size, which anticipate the instant claims. Moreover, the intended use for nerve regeneration is not given a patentable weight since the composition of the issued patents is the same as in the instant application and can perform the same function as in the instant claimed product. Thus, the instant and the issued patents claim a non-distinct invention of a

biodegradable composition or device comprising a polyhydroxyalkanoate (PHA) polymer that comprises 4-hydroxybutyrate (4HB or P4HB).

E. Claims 1 and 3-6 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 and 21-25 of copending Application No. 10/835926 (US2004/0234576, which has a common assignee), and claims 1-8 of copending Application No. 11/193580 (US2006/0058470, which has a common assignee). Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1 and 3-6 of the instant application encompass a nerve regeneration device comprising a polyhydroxyalkanoate polymer in the form of a porous conduit wherein the polyhydroxyalkanoate polymer comprises 4-hydroxybutyrate and the conduit comprises nerve cells, growth factors or drugs. Claims 1-18 and 21-25 of the '926 application encompass a fiber comprising poly-4-hydroxybutyrate polymers and the device comprising one or more fibers comprising poly-4-hydroxybutyrate for different medical uses including nerve regeneration. Claims 1-8 of the '580 application encompass a polymeric filament for a medical device comprising 4-hydroxybutyrate or copolymers thereof. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims recite the same composition comprising a polyhydroxyalkanoate polymer that comprises 4-hydroxybutyrate. In addition, the poly-4-hydroxybutyrate as recited in the claims also includes 4-hydroxybutyrate with one or more different hydroxy acid units. Furthermore, although

the claims in the issued patent do not specifically recite the pore size between 5-500μm and the shape, the working examples in these issued patents teach conduits and sheets and the pore size, which anticipate the instant claims. Moreover, the intended use of the device comprising 4-hydroxybutyrate for nerve regeneration is not given patentable weight since the composition of the copending applications is the same as in the instant application and can perform the same function as in the instant claimed product. Thus, the instant and the issued patents claim a non-distinct invention of a biodegradable composition comprising a polyhydroxyalkanoate polymer that comprises 4-hydroxybutyrate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

(10) Response to Argument

A. ((B)-(I) of the brief)

At p. 9 of the brief, Appellant argues that neither of the prior art references teaches the advantage of the P4HB for nerve regeneration. But Appellant acknowledges that Martin teaches P4HB artery repair fibrous mesh patches (sheet) with a pore size between 180-240μm for artery repair and Hadlock teaches a porous nerve regeneration conduit comprising P3HB with a pore size between 10-100μM. Appellants' arguments have been fully considered but they are not persuasive.

In contrast, the examiner asserts that the claimed conduit is obvious over the applied references. The applied references do teach a nerve conduit made of P4HB in a

form of a tube or sheet with a pore size between10-100 μm or between180-240μm in diameter. Briefly, Hadlock teaches a porous nerve regeneration conduit "comprising" biodegradable polymers of polyhydroxyalkanoate (PHA) with a pore size between 10-100 μm as it relates to instant claim 1 (see p.3; p. 7, 2nd paragraph; p. 14, claims 6-8) and Martin et al. teach P4HB patches (i.e. sheet) with a pore size between 180-240μm as it relates to instant claims 1, 3-5 (see p. 100, 1st col. 2nd paragraph). In addition, as described at the section of (9)-A., Martin also teaches that P4HB is more stable to hydrolysis than P3HB, and is useful for tissue engineering (i.e. including nerve regeneration). Furthermore, Hadlock teaches the nerve regeneration conduit comprising Schwann cells (i.e. neural cells) or neurotrophic agents and with a pore size between 10-100 μm (as it relates to instant claims 1 and 3-6; see p.2-4).

Although Hadlock does not teach 4HB or P4HB for nerve conduits, Martin et al. teaches that P4HB (i.e. a polymer of 4HB) is polyester that belongs to the class of polyhydroxyalkanoate (PHA) (i.e. comprises 4HB or P4HB) and for use in tissue regeneration; i.e. including nerve regeneration (see p.97, 1st col. 1st paragraph; 2nd col. 1st paragraph, in particular). Thus, it would have been obvious to a skilled artisan at the time the instant invention was made to use P4HB to replace P3HB to make or improve a nerve conduit and have expected success because P4HB is similar to P3HB and is more stable to hydrolysis than P3HB, and is useful for tissue engineering, including nerve regeneration.

In addition, although the pore size between180-240μm of the Martin's patches is not identical to the instant claims, the limitations of the pore size and the shape of

Martin's patches (sheet) are within the ranges as recited in instant claims, and therefore the claimed conduit are obvious over the disclosure of Martin's. Note that

"In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)", See MPEP 2144.05-I.

Furthermore, the intended use of the claimed invention in the preamble is not given patentable weight because the body of the claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations. In this case, the Martin's patches are within the limitation of the body of the claims, which is capable of performing the intended use as claimed.

At p. 10 of the brief, Appellant argues that the claimed conduits have an unexpectedly greater rate of nerve regeneration as compared to the prior art using P3HB or other polymeric nerve conduits (i.e. 1mm/day vs. 1mm/week, also see p.12 of the brief). Appellant argues that although Martin teaches P4HB for tissue regeneration, it does not include nerve, and thus no expectation of success to use P4HB among a big class of PHA. Appellant's arguments have been fully considered but they are not persuasive.

In response, the use of P4HB to replace P3HB to make or improve nerve conduits of Hadlock would have been obvious to a skilled artisan at the time the invention was made because the results of nerve regeneration using a nerve conduit made of P3HB are known, and the results of substituting P3HB with P4HB in a nerve conduit of Hadlock are also expected because Hadlock teaches a nerve regeneration

conduit "comprising" biodegradable polymers of PHA and Martin et al. teach that P4HB is similar to P3HB and is more stable and useful for tissue engineering (i.e. including nerve regeneration) and also teaches P4HB patches (i.e. sheet) with a pore size of 180-240μm as it relates to instant claims 1, 3-5 (see p. 100, 1st col. 2nd paragraph). Note that

"The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co.v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)" see MPEP§ 2144.07.

In addition,

"Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected results are evidence of unobviousness thereof." *In re Gershon*, 372 F.2d 535, 538, 152 USPQ 602, 604 (CCPA 1967). See MPEP 716.02(c)-II.

Furthermore,

"To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955, 128 USPQ 197 (CCPA 1960)." See MPEP 716.02(d)-II.

Appellant allegedly argues that the claimed conduits have unexpected results over the prior art. In contrast, Appellant's interpretation of 1mm/day in the instant vs 1mm/7days in the prior art is incorrect because the comparison should be under the same conditions, which should simultaneously and side-by-side measure the nerve growth at the same time, 7 days or 10 days using the instant conduit and the prior art conduit. It is known in the art, the length of nerve growth is linearly correlated to time; the nerve grows longer after a longer time. In this case, the measurement of the instant application was done at day 10 or 20 (see p. 10 and table 1 of the instant specification) and the measurement done by the prior art was at day 7. Thus, the total length of the

nerve growth is different at different days. The Appellant's conclusion does not support unexpected results as claimed.

Appellant fails to provide evidence of side-by-side comparisons to demonstrate unexpected results as claimed. No comparative data shows the unexpected results derived from a conduit made of P4HB in a shape and limitation as recited in instant claim 1 versus that of the closest prior art. No data demonstrate the unexpected results from different pore size versus a given pore size in the examples described within the specification (compared with Martin). Further, no data demonstrates a given structure of two sets of devices (instant vs. prior art) in a physical dimension would generate unexpected results as claimed. Note that

"Evidence of unexpected results must be weighed against evidence supporting *prima facie* obviousness in making a final determination of the obviousness of the claimed invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978)." See MPEP 716.02(c)-I.

Since Applicant fails to provide any evidence as discussed above to support any unexpected results as claimed, the claimed conduit is obvious over the prior art, absent evidence to the contrary.

B. & C. ((B)-(II) of the brief)

Note that U.S. Patent No. 6610764, US 6838493, US 6548569, US 6867247, and US 7179883 share the same specification, thus the reasons of the rejection and the citations are based on the reference of US6548569, which are also applied to all the cited references (i.e. issued patents and copending applications).

At p. 13-15 of the brief, Appellant argues that the instant claims are not obvious over the '569, '764, '493, '247 and '883 patents (Metabolix patents) and Seckel (the '885 patent) because there is no teaching of P4HB, no flexible material and no defined pore size particularly useful for nerve regeneration. At p. 14-15 of the brief, Appellant argues that the '569 patent teaches ways to alter rates of polymer degradation of the device not nerve regeneration. At p. 14 of the brief, Appellant argues that there is no disclosure and expectation of success to select the claimed pore size range for nerve regeneration. Appellant's arguments have been fully considered but they are not persuasive.

In contrast, Appellant's statements are incorrect with regard to the teachings of the '569 patent. The '569 patent does teach devices of tissue regeneration or nerve guidance/regeneration made of biocompatible polyhydroxyalkanoates (PHA) comprising poly-4-hydroxybutyrate (P4HB) as recited in instant claims 1 and 3-5 (see col. 4, lines 20-57; col.7, lines 31-35, in particular). Briefly, the '569 patent teaches a biodegradable device comprising a polyhydroxyalkanoate polymer comprising 4-hydroxybutyrate as a preferred embodiment (see col.7, lines 31-33, in particular) in a form of porous conduit such as having the shape of the nerve conduit products of NEUROTUBE^{TM} as incorporated by the references including US Patent NOs. 5735863, 5584885 and 5026381 (see col. 16, lines 42-52). The '569 patent teaches that the pore size of PHA is between nanometers to 500μm in diameter by using pore forming agents or particles with diameters between nanometers to 500 microns (i.e. as it relates to instant claims 4-5; see col. 10, lines 31-42, in particular). The '569 patent also teaches the process of

forming pore size of 80-180μm for nerve conduits made of P4HB using pore forming agents or particles (sodium chloride crystals) with diameters between 80-180μm (see col.33, example 4; col. 37, example 6).

Although the '569 patent does not teach the pore size between 5μm-500μm diameter, the range of pore size recited in the instant claims is obvious over the '569 patent because the claimed ranges (i.e. 5-500μm) overlap or lie inside ranges disclosed by the prior art (i.e. nanometer-500μm). Note that

"In the case where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)", See MPEP 2144.05-I.

In addition, the '569 patent shows that both of the conduits having the pore size with the ranges between nanometer-500μm and 80-180μm in diameter are effective for nerve guides, which would promote nerve regeneration. Since both of the conduits with a broader range and a narrower range of the pore size have the same effects on nerve regeneration, the recitation of the pore size between 5μm-500μm in the instant claims is an obvious variant because the results from the claimed conduits with the claimed pore size would predictably have the same result in nerve regeneration as in the prior art.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II.

Furthermore, the intended use of the claimed invention in the preamble is not given patentable weight because the body of the claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states the purpose or intended use of the invention, rather than any distinct definition of any of the claimed

invention's limitations. In this case, the Martin's patches are within the limitation of the body of the claims, which is capable of performing the intended use as claimed.

Although the '569 patent does not explicitly teach conduits comprises nerve cells, growth factors and drugs as recited in instant claim 6, Seckel (the '885 patent) teaches nerve guides (i.e. nerve conduits) or chambers comprising Schwann cells, growth factors and drugs as recited in instant claim 6 (see col.7, lines 18-col.8, lines 29; col. 16, lines 22-60, in particular). Thus, it would have been obvious to a skilled artisan at the time the instant invention was made to incorporate the teaching of Seckel to the teaching of the '569 patent to improve the nerve regeneration device of the '569 patent to enhance nerve regeneration with an expectation of success because Seckel has shown nerve guides or chambers comprising Schwann cells, growth factor and drugs can enhance nerve regeneration. Note that

"The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co.v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)" see MPEP§ 2144.07.

At p.15, Appellant argues that the evidentiary references (Schlossauer and Clavijo) related to NEUROTUBE™ are irrelevant. Appellant's arguments have been fully considered but they are not persuasive.

In contrast to Appellant's arguments, the teaching of Schlossauer and Cavijo about the property of NEUROTUBE™ is to support that the nerve guide of the '569 patent is in a shape of a tube with 2-8mm in diameter and 4cm in length and has the pore size of 30-50μm in diameter, which is within the limitation recited in instant claim 1.

At p. 16-17 of the brief, Appellant argues that the claimed conduits have an unexpectedly greater rate of nerve regeneration as compared to the prior art using P3HB or other polymeric nerve conduits (i.e. 1mm/day vs. 1mm/week, also see p.16 of the brief). Appellant's arguments have been fully considered but they are not persuasive.

In response, Appellant's arguments have been answered for the same reasons set forth above at section A with regard to unexpected results. In particular, Appellant has not supplied any evidence to show unexpected results. Briefly, Appellant's interpretation of 1mm/day in the instant vs 1mm/7days in the prior art is persuasive because the comparison should be done under the same condition, which should simultaneously and side-by-side measure the nerve growth at the same time. Appellant fails to provide evidence of side-by-side comparisons to demonstrate unexpected results as claimed. No comparative data shows the unexpected results derived from a conduit made of P4HB in a shape and limitation as recited in instant claim 1 versus the Metabolix patents. No data demonstrate the unexpected results from different pore size versus a given pore size in the examples described within the specification and within the Metabolix patents. Further, no data demonstrate a given structure of two sets of devices (instant vs. prior art) in a physical dimension would generate unexpected results as claimed. Thus, Appellant fails to provide sufficient evidence to support the unexpected results as claimed. Since Applicant fails to provide any evidence as discussed above to support any unexpected results as claimed, the claimed conduit is obvious over the prior art, absent evidence to the contrary.

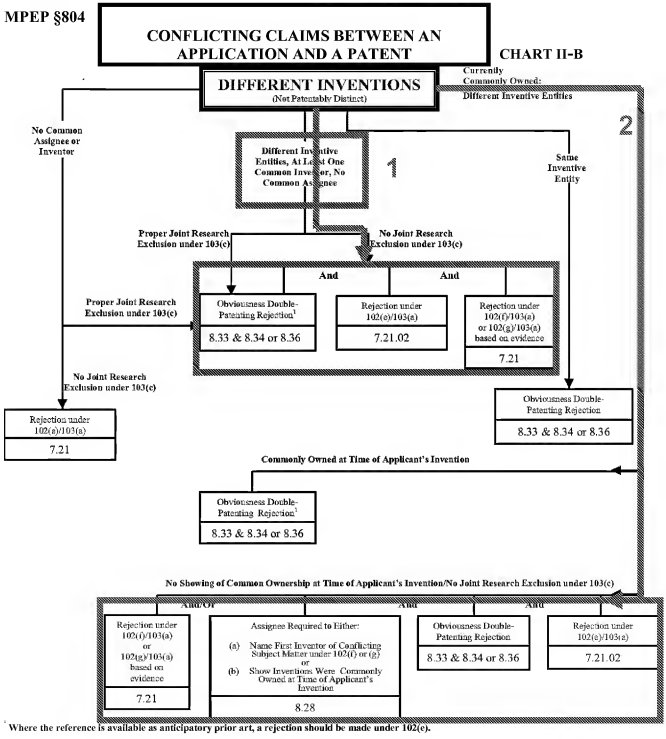
D. ((D)-(I) of the brief)

Note that U.S. Patent No. 6610764, US 6838493, US 6548569, US 6867247, and US 7179883 share a similar specification, thus the reasons of the rejection and the citations are based on the reference of US6548569, which are also applied to all the cited references (i.e. issued patents and copending applications).

At p. 20 of the brief, Appellant argues that the double patenting rejection is legally improper because US Patent Nos. 61610764, 6838493, 6548569, 6867247 and 7179883 and the instant application do not share a common ownership and are not under a joint research agreement. Appellant argues that the '764 patent (p.21-24), the 493 patent (p.24-25), the 569 patent (p. 26-27), the 247 patent (p. 27-29) and the '883 patent (p. 29-31) are owned by Metabolix, Inc. not by Tepha, Inc.. Appellant's arguments have been fully considered but they are not persuasive.

In response, although the cited US patents and the instant application do not share a common ownership (no common assignee) and have no joint research agreement (joint research exclusion), these cited patents and the instant application have a common inventor (**i.e. David Martin)**. The examiner asserts that the obvious double patenting (ODP) rejection is proper. Based on MPEP 804, the flow charts I-B and II-B for the double patenting rejection, the instant application and the cited patents have at least one common inventor, no common assignee and no joint research exclusion (see the highlight 1 in the Chart II-B below). Thus, it is proper to reject these

claims under the double-patenting rejection and also under the art rejection based on the Chart II-B below.



[1] Where the reference is available as anticipatory prior art, a rejection should be made under 102(e).

At p. 21-24 (the '764 patent), p. 24-25 (the '493 patent), p. 26-27 (the '569 patent), p. 27-29 (the '247 patent) and p. 29-31 (the '883 patent), Appellant further argues that although the specification teaches a biodegradable polyhydroxyalkanoate (PHA) polymer composition or device having a molecular weight between 10,000-10,000,000 Daltons for different tissue repair (including nerve guide, see p.25, p.28, p. 30) and having pore size between nanometers-500microns, the claims of these Metabolix patents do not specify a conduit for nerve regeneration with pore size between 5-500micron as claimed, and it is not proper to analyze the claims based on the specification. Appellant's arguments have been fully considered but they are not persuasive.

In contrast, based on MPEP 804, it is proper to use the portions of the disclosure (the specification) which provide support for the claims in the potentially conflicting patent or application. The examiner asserts that the instant claims are obvious over the claims of the cited patents because the examples in the cited patents are obvious over the claimed invention. It is noted that the preferable working examples in the specification of the '569 patent is a biodegradable device "comprising" a polyhydroxyalkanoate polymer comprising 4-hydroxybutyrate in a form of porous conduit such as a commercial conduit from the products of NEUROTUBE™ as described by the '569 patent (see col. 4, lines 20-57; col.7, lines 31-35; col. 16, lines 42-52, in particular), which is reasonably in the form of a tube as recited in instant claim 1. In addition, although the claims do not specify the conduit with a pore size between 5-500μm in diameter, the specification of the cited patents teaches a process of

generation of a conduit with a pore size between nanometer-500μm in diameter using pore forming agents or particles with diameters between nanometers to 500 microns (μm), and also teaches an example of generation of a pore size between 80-180μm for nerve conduits by using sodium chloride crystals, which are particles with diameters between 80-180μm (see for example, col. 33, line 40; col. 37, line 36 of the '569 patent). For example, the specification of the '569 patent teaches that the pore size of PHA is between nanometers to 500μm in diameter by using pore forming agents or particles with diameters between nanometers to 500 microns (i.e. as it relates to instant claims 4-5; see col. 10, lines 31-42 as in the '569 patent). The '569 patent also teaches a process of forming pore size between 80-180μm for a nerve conduit made of P4HB using pore forming agents or particles (sodium chloride crystals) with diameters between 80-180μm (see col.33, example 4; col. 37, example 6). Thus, the instant claims are obvious over the cited patents.

At p. 32-33 of the brief, Appellant argues that the claimed nerve regeneration device has an unexpected greater rate of nerve regeneration as compared to the prior art using P3HB or other polymeric nerve conduits (i.e. 1mm/day vs. 1mm/week, see p.33 of the brief). Appellant's arguments have been fully considered but they are not persuasive.

In response, it is noted that the cited patents teach a preferable biodegradable PHA composition or device comprising P4HB and the use of the composition or device for nerve regeneration, which is same as the claimed P4HB or 4HB as recited in instant

claims 1 and 3 (see col. 4, lines 20-57; col.7, lines 31-35; col. 16, lines 42-52, in particular). Although the pore size of the instant claims (i.e. 5-500μm) is different from the cited patents (i.e.nanometer-500μm and 80-180μm) are different, the cited pore size range is obvious over the cited patents because the range of the cited patents either overlap or within the claimed range. Note that

"where the claimed ranges 'overlap or lie inside ranges disclosed by the prior art' a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990)", See MPEP 2144.05-I.

In addition, Appellant has not supplied any evidence to show unexpected results. Note that

"To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955, 128 USPQ 197 (CCPA 1960)." See MPEP 716.02(d)-II

Appellant allegedly argues that the claimed conduits have unexpected results over the prior art. In contrast, Appellant fails to provide evidence of side-by-side comparisons to demonstrate unexpected results as claimed. No comparative data shows the unexpected results derived from a conduit made of P4HB in a shape and limitation as recited in instant claim 1 versus those of the cited patents. No data demonstrate the unexpected results from different pore size versus a given pore size in the examples described within the specification. Further, no data demonstrate a given structure of two sets of devices (instant vs. prior art) in a physical dimension would generate unexpected results as claimed.

"Evidence of unexpected results must be weighed against evidence supporting *prima facie* obviousness in making a final determination of the obviousness of the claimed invention. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978)." See MPEP 716.02(c)-I.

Since Applicant fails to provide any evidence as discussed above to support any unexpected results as claimed, the claimed conduit is obvious over the prior art, absent evidence to the contrary.

E. ((D)-(II) of the brief)

Note that US 6548569 and copending Application Nos. 10/835926 (US2004/0234576) and 11/193580 (US2006/0058470) share a similar specification, thus the reasons of the rejection and the citations are based on the reference of US6548569, which are also applied to all the cited references (i.e. issued patents and copending applications).

At p. 33 of the brief, Appellant argues that the ODP rejection is moot because claims 1-18 and 21-25 of the '576 application (US2004/0234576) have been canceled. At p. 34 of the response, the rejection is moot because claims 1-8 of the '470 application (US2006/0058470) are not under examination. Appellant's arguments have been fully considered but they are not persuasive.

In response, although claims 1-18 and 21-25 of US2004/0234576 have been canceled, the newly added claims 26-45 encompass a biodegradable composition or device comprising P4HB and the properties of the composition or device are based on the teachings of the '569 patent (see p.1, [0004]). Thus, US2004/0234576 and the instant claimed a non-distinct invention overlapping in scope.

In addition, although claims 1-8 are not under examination, claims 9-16 of US2006/0058470 encompass a biodegradable composition or device comprising P4HB

and the properties of the composition or device are based on the teachings of the '569 patent (see p.1, [0004]). Thus, US2006/0058470 and the instant claimed a non-distinct invention overlapping in scope. Although US2004/0234576 and US2006/0058470 and the instant application have different inventive entities, they have a common assignee. Thus, the ODP rejection is also proper based on the Charts I-B & II-B (see the highlight 2 in the Chart II-B below) and for the reason given above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Chang-Yu Wang, Ph.D.
Examiner
Art Unit 1649

/CYW/
August 8, 2008

Conferees:

Christine Saoud, Ph.D., Primary Examiner

/Christine J Saoud/
Primary Examiner, Art Unit 1647

Jeffrey Stucker, SPE 1649

/Jeffrey Stucker/
Supervisory Patent Examiner, Art Unit 1649

/Robert A. Wax/
Robert A. Wax
Quality Assurance Specialist
Technology Center 1600